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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/663,555 | 09/16/2003 | Bruce Shull | 1718-0004 | 2589 |

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| EXAMINER | |
|---|---|
| WOOD, AMANDA P | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1655 | |

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/663,555 | SHULL ET AL. | |
| | Examiner | Art Unit | |
| | Amanda P. Wood | 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3 and 9-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**DETAILED ACTION- Final Rejection**

The amendment filed 17 January 2006 is acknowledged and has been entered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 102***

Claims 1-3 and 9-10 stand rejected under 35 U.S.C. 102(e) as being anticipated by Goldman (US 6,844,149) for the reasons set forth in the previous Office action which are restated below.

Goldman teaches a multi-component test strip (i.e., a test strip having at least two sample analysis regions, or stacks, and each stack having one or more layers) for analyzing a plurality of blood components (i.e., cholesterol) in a single blood sample (see, for example, column 12, lines 20-31). The term "stack," as used by Applicant, in its broadest reasonable interpretation, can be deemed a sample analysis region or pad, as described by Goldman (see, for example, column 12, lines 21-35). Furthermore, Goldman teaches the use of a layer or membrane to separate plasma from whole blood (i.e., a blood separation layer) and another layer having reagents incorporated within that will produce a colored reaction in proportion to the concentration of the blood component tested for (see, for example, column 27, lines, 10-60). Among the specific blood components Goldman describes are total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol (see, for example, column 13, lines 1-10).

Furthermore, Goldman specifically teaches that health advocacy groups and respected medical centers recommend testing total cholesterol, HDL, and triglycerides (i.e., non-LDL cholesterol) wherein total cholesterol is made up of LDL, HDL, and other blood cholesterol particles (see, for example, col. 2, lines 5-60). Therefore, one of ordinary skill in the art can appreciate that by measuring total cholesterol in one stack and measuring non-LDL cholesterol in a second stack, the level of LDL cholesterol can be determined from the test strip described by Goldman.

Additionally, with reference to Thakore et al, Goldman teaches that "precise...temperature controls are not necessary" because the method of using this dry test strip for cholesterol testing measures an end-point of the reaction (see, for example, Goldman, column 27, lines 30-60). Therefore, broadest reasonable interpretation of the phrase "precise...temperature controls are not necessary" can be interpreted to mean that a reaction may be practiced at room temperature, a limitation provided by applicant in Claim 2.

Therefore, the cited reference is still deemed to anticipate the instant claims above.

Applicants' arguments concerning the above USC 102 rejection have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicants argue that the cited references fail to teach or suggest that the concentration of LDL cholesterol is determine by subtracting the results from one of the stacks from the other of the stacks. However, as Goldman specifically teaches in Column 2, lines 5-60, it is well-known in the art that total cholesterol and HDL and other non-LDL

cholesterol are the recommended tests for cholesterol, and therefore, one of ordinary skill in the art can appreciate that LDL cholesterol can then be determined from subtracting the results of one test from the other. Furthermore, Applicant argues that each of claims 2, 3 and 9-11 contains a limitation not found in Goldman. It is unclear to what limitations Applicant is referring.

***Claim Rejections - 35 USC § 103***

Amended Claims 1-3 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldman (U.S. Patent 6,844,149 B2) in view of Carroll et al (U.S. Patent 6,284,550) and Nakamura et al (US Patent 6,764,828 B2) for the reasons set forth in the previous Office action which are restated below.

Goldman is relied upon for the reasons set forth above.

Goldman does not expressly teach a method wherein a pseudo-end point is used to measure LDL cholesterol.

Carroll et al beneficially teach the use of a multi-layered test strip for measuring the amount of a suspected analyte (i.e., cholesterol) in a fluid, such as whole blood, whereby a color change in the strip corresponds to the amount of analyte in the fluid. Carroll et al also teaches the use of a separating layer in a test strip device to remove red blood cells from whole blood (see, for example, column 2, lines 1-20, and 45-61). Further, Carroll et al teach the use of a reflectance meter to measure the amount of change in reflectance of the color on the test strip so that the end-point of the reaction can be determined. In particular, Carroll et al beneficially teach that an "end-point" of

the reaction is reached when successive reflectance readings taken at 5 second increments differ by less than 5% --i.e., the measurement is taken after the reaction has substantially stopped (see, for example, col. 8, lines 25-55). While Carroll et al discuss in detail the measurement of glucose by this method, they also state that by "modifying the chemical reagent solutions" used in the test strip, one can test for the presence and/or amount of such analytes as cholesterol (see, for example, column 2, lines 24-67).

Goldman and Carroll et al do not expressly teach the use of a surfactant that acts on non-LDLs.

Nakamura et al. beneficially teach the use of a surfactant such as Emulgen B66 that preferentially reacts with HDL and VLDL cholesterol (i.e., non-LDL cholesterol). Nakamura et al. further beneficially discloses that a cholesterol-assaying enzyme reagent used in the presence of a specific surfactant to HDL and VLDL actually accelerates the reaction of HDL and VLDL cholesterol and retards the reaction of LDL cholesterol (see, e.g., Abstract; col. 2, lines 325-67; and col. 3, lines 30-65). In addition, Nakamura et al. state that the reaction of HDL and VLDL cholesterol terminates prior to the reaction of LDL cholesterol – thus, adding a surfactant so as to facilitate the measurement of the reaction end-point to determine the amount of non-LDL cholesterol contained in the plasma tested would be clearly desirable.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the blood cholesterol test strips disclosed by Goldman, based upon the beneficial teachings provided by Carroll et al, with respect to

recognized method of using an end-point or pseudo-end point reaction taken by a reflectance meter, and by Nakamura et al, with respect to the art-recognized method of adding a surfactant that acts on non-LDL cholesterol preferentially to acting on LDL cholesterol, as discussed above. In particular, Goldman teaches that it is well-known in the art to determine total cholesterol and non-LDL cholesterol as a part of routine medical testing, whereby it can be appreciated that one of ordinary skill in the art could determine a patient's level of LDL cholesterol by testing these two parameters and subtracting one from the other. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to include and/or substitute a surfactant such as Emulgen B66 that acts on HDL and other non-LDL cholesterol within cholesterol test strips such as those taught by the primary references (e.g., for assaying non-LDL levels) based upon the beneficial teachings provided by Nakamura et al. (as discussed above) – i.e., a surfactant that acts on HDL (e.g., Emulgen B66) or on other non-LDLs so that the non-LDL fraction of the blood sample plasma would react faster than the LDL fraction of the sample, based upon the art-recognized ability of a surfactant to aid in the quantification of specific lipoproteins. One would have been motivated to add a surfactant such as Emulgen B66 to the test strip of Goldman for the expected benefit of reacting non-LDL cholesterol prior to and more quickly than reacting LDL cholesterol, so as to obtain an pseudo-end-point measurement of non-LDL cholesterol before LDL cholesterol has reacted, as beneficially taught by the Carroll et al and Nakamura et al. The result-effective adjustment of particular conventional working conditions and/or design-choice

parameters within such blood cholesterol test strips/assays (e.g., using a particular end-point algorithm, and/or matrix design arrangement therein) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Applicants' arguments concerning the above USC 103 rejection have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicants argue that the cited references fail to teach or suggest that the concentration of LDL cholesterol is determine by subtracting the results from one of the stacks from the other of the stacks. However, as Goldman specifically teaches in Column 2, lines 5-60, it is well-known in the art that total cholesterol and HDL and other non-LDL cholesterol are the recommended tests for cholesterol, and therefore, one of ordinary skill in the art can appreciate that LDL cholesterol can then be determined from subtracting the results of one test from the other. Furthermore, Applicant argues that each of claims 2, 3 and 9-11 contains a limitation not found in Goldman or in Carroll et al. It is unclear to what limitations Applicant is referring. In addition, Applicant argues that the combination of references teach that LDL should be measured by allowing the

reaction to proceed for a specific time kinetically monitoring a subsequent reaction or by adding an additional reaction accelerating reagent. However, this argument is not found persuasive because Goldman anticipates the claimed invention while Carroll et al provide motivation to use an end-point or pseudo-end point measurement of cholesterol so that timing the reaction is not necessary. Furthermore, Nakamura et al beneficially provide both motivation and the means to facilitate a faster reaction of non-LDL cholesterol by using a surfactant such as Emulgen B66, which reacts with non-LDL cholesterol substantially faster than it does with LDL cholesterol. Applicant's argument that Nakamura et al teach away from the instant invention is not found persuasive because Nakamura et al specifically state in Column 4, lines 5-20 that any known enzymatic assay method may be used for assaying cholesterols and that a surfactant such as Emulgen B66 may be added to the reagents used in those methods. In conclusion, it would have been obvious to one of ordinary skill in the art to combine Goldman's test strip with the methods employed by Carroll et al and Nakamura et al to create a faster and simpler method of determining LDL cholesterol without the need for timing.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

**Conclusion**

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on M-F 9:30AM -5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey, can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

APW
Examiner
Art Unit 1655

APW

CHRISTOPHER R. TATE
PRIMARY EXAMINER